

3. The method of claim 2, wherein said TNF inhibitor is encoded by a nucleic acid sequence selected from the group consisting of:

- (i) the DNA sequence as shown in Fig. 32 or a coding portion thereof;
- (ii) the DNA sequence as shown in Fig. 39 or a coding portion thereof;
- (iii) the DNA sequence as shown in Fig. 40 or a coding portion thereof;
- (iv) the DNA sequence as shown in Fig. 56 or a coding portion thereof;
- (v) the DNA sequence as shown in Fig. 58 or a coding portion thereof;
- (vi) a sequence which is degenerate in the coding regions or portions thereof of (i), (ii), (iii), (iv) and (v);
- (vii) a sequence which hybridizes to a sequence complementary to (i), (ii), (iii), (iv), (v) or (vi); and
- (viii) a sequence which is complementary to (i), (ii), (iii), (iv), (v), (vi) or (vii).

4. The method of claim 3 wherein said TNF mediated disease is selected from the group consisting of arthritis, bowel necrosis, cachexia, leukemias and septic shock.

5. DNA encoding a TNF inhibitor selected from the group consisting of:

- (i) the DNA sequence as shown in Fig. 32 or a coding portion thereof;
- (ii) the DNA sequence as shown in Fig. 39 or a coding portion thereof;
- (iii) the DNA sequence as shown in Fig. 40 or a coding portion thereof;

- (iv) the DNA sequence as shown in Fig. 56 or a coding portion thereof;
- (v) the DNA sequence as shown in Fig. 58 or a coding portion thereof;
- (vi) a sequence which is degenerate in the coding regions or portions thereof of (i), (ii), (iii), (iv) and (v);
- (vii) a sequence which hybridizes to a sequence complementary to (i), (ii), (iii), (iv), (v) or (vi); and
- (viii) a sequence which is complementary to (i), (ii), (iii), (iv), (v), (vi) or (vii).

6. A nucleic acid encoding a TNF inhibitor, said TNF inhibitor comprising an amino acid sequence selected from the group consisting of:

- (i) an amino acid sequence as shown in Figure 38 or a fragment thereof;
- (ii) an amino acid sequence as shown in Figure 56 or a fragment thereof;
- (iii) an amino acid sequence as shown in Figure 57 or a fragment thereof;
- (iv) an amino acid sequence as shown by residues 1 through 182 (40kDa inhibitor $\Delta 53$) in Figure 57 or a fragment thereof; and
- (v) an amino acid sequence as shown by residues 1 through 184 (40kDa inhibitor $\Delta 51$) in Figure 57 or a fragment thereof.

7. A TNF inhibitor which is non-glycosylated and has a molecular weight of about 18kDa.

8. A TNF inhibitor produced in a host cell not capable of glycosylation or a non-human host cell capable of glycosylation and encoded by a nucleic acid sequence comprising a sequence selected from the group consisting of:

- (i) the DNA sequence as shown in Fig. 32 or a coding portion thereof;
- (ii) the DNA sequence as shown in Fig. 39 or a coding portion thereof;
- (iii) the DNA sequence as shown in Fig. 40 or a coding portion thereof;
- (iv) the DNA sequence as shown in Fig. 56 or a coding portion thereof;
- (v) the DNA sequence as shown in Fig. 58 or a coding portion thereof;
- (vi) a sequence which is degenerate in the coding regions or portions thereof of (i), (ii), (iii), (iv) and (v); and
- (vii) a sequence which hybridizes to a sequence complementary to (i), (ii), (iii), (iv), (v), or (vi).

9. A TNF inhibitor produced in a host cell not capable of glycosylation or a non-human host cell capable of glycosylation, said TNF inhibitor comprising an amino acid sequence selected from the group consisting of:

- (i) an amino acid sequence as shown in Figure 38 or a fragment thereof;

- (ii) an amino acid sequence as shown in Figure 56 or a fragment thereof;
 - (iii) an amino acid sequence as shown in Figure 57 or a fragment thereof;
 - (iv) an amino acid sequence as shown by residues 1 through 182 (40kDa inhibitor Δ 53) in Figure 57 or a fragment thereof; and
 - (v) an amino acid sequence as shown by residues 1 through 184 (40kDa inhibitor Δ 51) in Figure 57 or a fragment thereof.
10. A composition comprising the TNF inhibitor of claim 8 in a slow release formulation.
11. A lyophilized powder comprising the TNF inhibitor of claim 8.
12. The lyophilized powder of claim 11, further comprising a pharmaceutically acceptable carrier.
13. A kit for preparing an aqueous pharmaceutical formulation comprising the lyophilized powder of claim 11 and a physiologically acceptable solvent.
14. A host cell containing a recombinant DNA molecule comprising a nucleic acid sequence defined in claim 5.
15. A process for preparing a recombinant TNF inhibitor polypeptide, comprising producing the recombinant TNF inhibitor polypeptide in a host cell according

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to claim 14 under suitable conditions to express the recombinant DNA molecule contained therein to produce the recombinant polypeptide.

~~16. The process of claim 15, further comprising harvesting the TNF inhibitor~~

17. A substantially purified interleukin-1 inhibitor (IL-1i), comprising a glycosylated or nonglycosylated polypeptide, said polypeptide being capable of inhibiting IL-1 and being sufficiently pure such that at least a portion of the amino acid sequence of said polypeptide can be determined, wherein said polypeptide is selected from the group consisting of

A) a polypeptide comprising all or an IL-1 inhibitory fragment of the amino acid sequence:

(U) (X) P S G R K S S K M Q A F R I W D V N Q K T F Y L R N
N Q L V A G Y L Q G P N V N L E E K I D V V P I E P H A
L F L G I H G G K M C L S C V K S G D E T R L Q L E A V
N I T D L S E N R K Q D K R F A F I R S D S G P T T S F
E S A A C P G W F L C T A M E A D Q P V S L T N M P D E
G V M V T K F Y F Q E D E

wherein (U) is M or nothing and (X) is R or P; and

B) a polypeptide that is at least about 70% homologous to the amino acid sequence set forth in A).

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18. A composition comprising the IL-1i of claim 17 in a slow release formulation.

19. A lyophilized powder comprising a polypeptide capable of inhibiting interleukin-1 (IL-1) and being sufficiently pure such that at least a portion of the amino acid sequence of said polypeptide can be determined, wherein said polypeptide is methionylated or non-methionylated and has an amino acid sequence that is at least 70% homologous to the following amino acid sequence:

(U) (X) P S G R K S S K M Q A F R I W D V N Q K T F Y L R N
N Q L V A G Y L Q G P N V N L E E K I D V V P I E P H A
L F L G I H G G K M C L S C V K S G D E T R L Q L E A V
N I T D L S E N R K Q D K R F A F I R S D S G P T T S F
E S A A C P G W F L C T A M E A D Q P V S L T N M P D E
G V M V T K F Y F Q E D E

wherein (U) is M or nothing and (X) is R or P.

20. The lyophilized powder of claim 19, further comprising a pharmaceutically acceptable carrier.

21. A kit for preparing an aqueous pharmaceutical formulation comprising the lyophilized powder of claim 19 and a physiologically acceptable solvent.

An isolated nucleic
22. ~~A nucleic acid sequence encoding an interleukin-1 inhibitor (IL-1i)~~

Sub 10
polypeptide, said polypeptide being capable of inhibiting IL-1, wherein said polypeptide is selected from the group consisting of

A) a polypeptide comprising all or an IL-1 inhibitory fragment of the amino acid sequence:

(U) (X) P S G R K S S K M Q A F R I W D V N Q K T F Y L R N
N Q L V A G Y L Q G P N V N L E E K I D V V P I E P H A
L F L G I H G G K M C L S C V K S G D E T R L Q L E A V
N I T D L S E N R K Q D K R F A F I R S D S G P T T S F
E S A A C P G W F L C T A M E A D Q P V S L T N M P D E
G V M V T K F Y F Q E D E

wherein (U) is M or nothing and (X) is R or P and

B) a polypeptide that is at least about 70% homologous to the amino acid sequence set forth in A).

Sub B2
23. ~~A host cell containing a recombinant DNA molecule comprising a nucleic acid sequence defined in claim 22.~~

24. A process for preparing an interleukin-1 inhibitor (IL-1i) polypeptide, comprising producing the recombinant IL-1i polypeptide in a host cell according to claim 23 under suitable conditions to express the recombinant DNA molecule contained therein to produce the recombinant polypeptide.

25. The process of claim 24, further comprising harvesting the IL-1i polypeptide.

~~26. A composition comprising a water-soluble polymer comprising a reactive Michael acceptor.~~

27. A composition of claim 26, wherein said polymer further comprises a second reactive Michael acceptor or a reactive NHS-ester.

28. A composition of claim 26, wherein said Michael acceptor is maleimide.

29. A composition of claim 26, wherein said Michael acceptor is vinyl sulfone.

30. A composition of claim 26, wherein said polymer further comprises a reactive NHS-ester and wherein said Michael acceptor is maleimide.

31. A composition of claim 26, wherein said polymer further comprises a reactive NHS-ester and wherein said Michael acceptor is vinyl sulfone.

32. A composition of claim 26, further comprising a biologically-active molecule conjugated to said polymer.

33. A composition of claim 32, wherein the Michael acceptor is a sulfone moiety and said biologically-active molecule has a reactive thiol moiety, and wherein said sulfone moiety forms a linkage with said thiol moiety.

34. A composition of claim 33, wherein said sulfone moiety is vinyl sulfone.

35. A composition of claim 32, wherein said biologically-active molecule is a tumor necrosis factor (TNF) inhibitor.